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VARYING BOUNDARY CONDITIONS

WITH LARGE DIFFUSIVITY

by

Jack K. Hale and Carlos Rocha

March 1985 LCDS #85-5

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For systems of semilinear parabolic partial differential equations on bounded domains with large diffusivity and homogeneous boundary conditions close to the Neumann conditions we associate a system of ordinary differential equations (ode's) from which the dynamics of the original system can be inferred. Small perturbations of the Neumann case produce large perturbations inthe ode's with corresponding effects on the dynamics of the system. The same theory is valid for functional differential equations. Applications are considered in models for control by genetic repression of biological material in cells.

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VARYING BOUNDARY CONDITIONS WITH LARGE DIFFUSIVITY

by

Jack K. Hale and Carlos Rocha

ABSTRACT

For systems of semilinear parabolic partial differential equations on bounded domains with large diffusivity and homogeneous boundary conditions close to the Neumann conditions, we associate a system of ordinary differential equations (ode's) from which the dynamics of the original system can be inferred. Small perturbations of the Neumann case produce large perturbations in the ode's with corresponding effects on the dynamics of the system. The same theory is valid for functional differential equations. Applications are considered in models for control by genetic repression of biological material in cells.

1. Introduction.

Consider the system of parabolic partial differential equations (PDE)

$$(1.1)\qquad \partial u/\partial t = D\Delta u + f(u); \quad x \in \Omega$$

$$(1.2)\qquad \partial u/\partial n = E(x)u; \quad x \in \partial\Omega$$

where $u \in \mathbb{R}^N$, $\Omega \subset \mathbb{R}^n$, $n \le 3$, is a bounded open set with $\partial\Omega$ smooth, $D = \mathrm{diag}(d_1,\ldots,d_N)$, $E = \mathrm{diag}(e_1,\ldots,e_N)$ where each $d_j > 0$ is constant and each $e_j\colon \partial\Omega \to \mathbb{R}$ is continuous. Also, suppose that $f\colon \mathbb{R}^N \to \mathbb{R}^N$ is a $C^{1,1}$-function; that is, is continuous and has a Lipschitz continuous first derivative.

Our objective is to study the behavior of solutions of (1.1), (1.2) when D^{-1}, E are small; that is, the boundary conditions are close to homogeneous Neumann conditions and the diffusivity is large.

To state the results, we need some terminology. If $X = L^2(\Omega,\mathbb{R}^N)$,

$$D(A) = \{\phi \in W^{2,2}(\Omega,\mathbb{R}^N)\colon \ \partial\phi/\partial n = E\phi \ \text{ on } \ \partial\Omega\}$$

then $A\phi = -D\Delta\phi$ is a sectorial operator and one can define the fractional powers A^α of A, $0 \le \alpha$ and the space $X^\alpha = D(A^\alpha)$ with the graph norm. If $3/4 < \alpha < 1$, then $X^\alpha \subset W^{1,2}(\Omega,\mathbb{R}^N) \cap L^\infty(\Omega,\mathbb{R}^N)$

with continuous inclusion. One can then show that (1.1), (1.2) defines a local $C^{1,1}$-semigroup $T_{D,E}(t)$ on X^α for $3/4 < \alpha < 1$ (see, for example, Henry [9,p.75]).

For any set $B \subset X^\alpha$, the ω-limit set $\omega(B)$ of B is defined as $\omega(B) = \cap_{\tau \geq 0} C\ell \cup_{t \geq \tau} T_{D,E}(t)B$. A set $B \subset X^\alpha$ is said to be invariant if, for any $\phi \in B$, one can define $T_{D,E}(t)\phi$ for $t \in \mathbb{R}$ and $T_{D,E}(t)\phi \in B$ for $t \in \mathbb{R}$. A set $A \subset X^\alpha$ is said to be a compact attractor for (1.1), (1.2) if A is compact, invariant and there is a neighborhood B of A such that $\omega(B) \subset A$.

Under the assumption that the ordinary differential equation

$$du/dt = f(u) \tag{1.3}$$

has a compact attractor A, it was shown in Hale [5] that A is a compact attractor for (1.1), (1.2) if $E = 0$ provided that $d\lambda$ is sufficiently large, where $d = \min(d_1,\ldots,d_N)$ and λ is the first eigenvalue of $-\Delta$ with homogeneous Neumann conditions. In other words, (1.1), (1.2) with $E = 0$ behaves qualitatively as the ODE (1.3) if $d\lambda$ is large.

We will obtain an appropriate generalization of this result when D^{-1}, E are small; that is, the qualitative properties of the flow for (1.1), (1.2) can be determined from an ODE under certain hypotheses.

At first, it is instructive to guess the appropriate ODE. If $\bar{u}(t) = |\Omega|^{-1}\int_\Omega u(t,x)dx$ and $u(t,x)$ is a solution of (1.1), (1.2),

then, by integrating (1.1) and using the boundary conditions (1.2), one obtains

$$\frac{d\bar{u}}{dt} = D|\Omega|^{-1}\int_{\partial\Omega} E(x)u(t,x)dx + |\Omega|^{-1}\int_{\Omega} f(u(t,x))dx.$$

If we assume that

$$E(x) = E(x,D),$$

$$(1.4) \qquad D|\Omega|^{-1}E(x) \to \tilde{E}(x), \quad \tilde{E}(x) \text{ continuous},$$

$$\int_{\partial\Omega} \tilde{E}(x)dx = \zeta$$

and $u(t,x) - \bar{u}(t) \to 0$ as $d = \min(d_1,\dots,d_N) \to \infty$, then $v = \lim_{d\to\infty} \bar{u}$ satisfies the (ODE)

$$(1.5) \qquad \frac{dv}{dt} = \zeta v + f(v) \overset{\text{def}}{=} g(v,\zeta)$$

The "perturbation" $E(x,D)$ in the boundary conditions leads to the perturbation ζv in the vector field $f(v)$ in (1.3).

Under the assumption (1.4), there are N eigenvalues $\lambda_1(D), \dots,\lambda_N(D)$ of $D\Delta$ with boundary conditions (1.2) and corresponding unit eigenfunctions $\phi_1(D),\dots,\phi_N(D)$ such that

$$\Lambda_D = \mathrm{diag}(\lambda_1(D),\dots,\lambda_N(D)) \to \zeta$$

$$\Phi_D = (\phi_1(D),\dots,\phi_N(D)) \to |\Omega|^{-\frac{1}{2}}I, \quad I = \text{identity}$$

as $d \to \infty$. Decompose X^α as

$$X^\alpha = U \oplus U_\alpha^\perp$$

$$U = \{\phi = \Phi_D v : v \in \mathbb{R}^N\}$$

$$U_\alpha^\perp = \{\psi \in X^\alpha : \langle\psi,\phi\rangle = 0 \text{ for all } \phi \in U\}$$

where $\langle\psi,\phi\rangle = \int_\Omega \psi^T(x)\phi(x)dx$.

If $u(t,x)$ is a solution of (1.1), (1.2) and

$$(1.6) \qquad u(t,x) = \Phi_D v + w(t,x), \quad w(t,\cdot) \in U_\alpha^\perp$$

then

$$(1.7a) \qquad dv/dt = \Lambda_D v + \int_\Omega \Phi_D f(\Phi_D v+w)$$

$$(1.7b) \qquad \partial w/\partial t = D\Delta w + f(\Phi_D v+w) - \Phi_D \int_\Omega \Phi_D f(\Phi_D v+w) \quad \text{on } \Omega$$

$$\partial w/\partial n = Ew \quad \text{on } \partial\Omega$$

The main result of the paper is the following.

<u>Theorem 1.1.</u>

<u>Suppose</u> $D, E(\cdot,D)$ <u>satisfy</u> (1.4) <u>and the ODE</u> (1.5) <u>has a compact attractor</u> $A_{\Lambda,f}$ <u>with</u> $V \subset \mathbb{R}^N$ <u>being a neighborhood of</u> $A_{\Lambda,f}$ <u>such that</u>

$\omega(V) \subset A_{\zeta,f}$. Then, for any neighborhood W of $A_{\zeta,f}$ with $C\ell W \subset V$, there is a constant $d_0 > 0$ and a C^1-function $h: W \times \{D: d > d_0\} \to U_\alpha^\perp$ such that $h(v,D) \to 0$ as $d \to \infty$ and the set

$$(1.8) \qquad M_D = \{u = \Phi_D v + h(v,D),\ v \in W\}$$

is an exponentially asymptotically stable invariant manifold for (1.1), (1.2). Furthermore, the flow on this manifold is given by $u(t,x) = \Phi_D(x)v(t) + h(v(t),D)(x)$ where $v(t)$ is a solution of the ODE

$$(1.9) \qquad dv/dt = \Lambda_D v + \int_\Omega \Phi_D f(\Phi_D v + h(v,D)) \overset{\text{def}}{=} \Lambda_D v + G(D,v)$$

The proof of this theorem is given in Section 2. It is interesting to note some implications of this result.

Since $\Lambda_D \to \zeta$, $\Phi_D \to |\Omega|^{-\frac{1}{2}}I, h(v,D) \to 0$ as $d \to \infty$, relation (1.6) shows that the average $\bar{u}$ of u approaches $|\Omega|^{-\frac{1}{2}}v$ and v satisfies the ode

$$(1.10) \qquad dv/dt = \zeta v + |\Omega|^{\frac{1}{2}} f(|\Omega|^{-\frac{1}{2}}v)$$

A rescaling of $v \to |\Omega|^{\frac{1}{2}}v$ yields (1.5).

The compact attractor $A_{\zeta,f}$ is upper semicontinuous in the Hausdorff metric with respect to C^1-perturbations of the vector

field $\zeta v + f(v)$ (see, for example, Hale [6]). The flow defined by (1.9) is equivalent to the flow defined by rescaling $v \to |\Omega|^{\frac{1}{2}} v$. The new vector field $A_D v + |\Omega|^{-\frac{1}{2}} G(D, |\Omega|^{\frac{1}{2}}$ approaches the vector field $g(v,\zeta) = \zeta v + f(v)$ in the C^1 topology in W as $d \to \infty$. Thus, (1.9) has a compact attractor $A_{D,\zeta,f}$ in W and $\lim_{d\to\infty} A_{D,\zeta,f} \subset A_{\zeta,f}$ as $d \to \infty$. If the flow of (1.5) on $A_{\zeta,f}$ is structurally stable in W, then $\lim_{d\to\infty} A_{D,\zeta,f} = A_{\zeta,f}$ and the flow defined by (1.9) is equivalent to the flow defined by (1.5) in W. This is summarized in

Corollary 1.2. *For* $d > d_0$, *equation* (1.9) *has a compact attractor* $A_{D,\zeta,f}$ *in* W, $\lim_{d\to\infty} A_{D,\zeta,f} \subset A_{\zeta,f}$. *If the flow defined by* (1.5) *is structurally stable on* $A_{\zeta,f}$ *in* W, *then the flow defined by* (1.9) *is structurally stable on* $A_{D,\zeta,f}$ *in* W *and is equivalent to* (1.5) *in* W.

The following observation is also important. Although the perturbation $E(\cdot,D) \to 0$ as $d \to \infty$, the behavior of the flow defined by (1.1) cannot be considered as a small perturbation of the flow defined by Neumann boundary conditions. In fact, the matrix ζ can be very large and therefore the flows defined by (1.3) and (1.5) can be very different. An illustration will be given in Section 3. The flow defined by (1.1) is close to the flow defined by the equation

$$\frac{\partial u}{\partial t} = D\Delta u + f(u), \quad x \in \Omega$$

$$\frac{\partial u}{\partial n} - D^{-1}|\Omega||\partial\Omega|^{-1} \zeta u = 0, \quad x \in \partial\Omega$$

for d large. The similarity with Neumann boundary conditions is that the eigenfunctions corresponding to the eigenvalues close to ζ are approximately constant functions for d large and so the average of u satisfies (1.5).

Equation (1.1) may also contain other physical parameters which vary over some set. In such a case, equation (1.5) would also contain these parameters and the flow may undergo various types of bifurcations as the parameters vary. It would then be of interest to relate these bifurcations for the limit equation to bifurcation of (1.9) for the flow of (1.1) on the attractor. For example, suppose $f = f(u,r)$, $r \in \mathbb{R}$, and the limit equation (1.5) with f replaced by $f(u,r)$ has an attractor $A_{\zeta,r}$ which is a point v_0 for $r \leq 0$ and there is a generic supercritical Hopf bifurcation at $r = 0$; that is, the attractor $A_{\zeta,r}$ is a disk for $r > 0$ with the boundary of $A_{\zeta,r}$ being a stable periodic orbit which attracts all points on $A_{\zeta,r}$ except the equilibrium point. Equation (1.9) will also contain r,

$$(1.9)_r \qquad dv/dt = \Lambda_D v + G(D,v,r)$$

where $\Lambda_D \to \zeta$, $G(D,v,r) \to f(v,r)$ as $d \to \infty$ uniformly for $|r| \leq r_0$ and $v \in V$ for some fixed $r_0 > 0$ and neighborhood V of $\cup_{|r|\leq r_0} A_{\zeta,r}$.

This convergence will be in the C^k topology if f is $C^{k,1}$. Furthermore, the attractor $A_{D,\zeta,r}$ satisfies $\lim_{d\to\infty} A_{D,\zeta,r} \subset A_{\zeta,r}$, $|r| \le r_0$. These remarks are immediate consequences of the proof of Theorem 1.1 below. Therefore, if we fix $d \ge d_0$, with d_0 sufficiently large, the one parameter family of flows defined by the vector fields in $(1.9)_r$, $|r| \le r_0$, have the property that there is an $\tilde{r}(D)$, $|\tilde{r}(D)| < r_0$, $\tilde{r}(D) \to 0$ as $d \to \infty$, such that the attractor $A_{D,\zeta,r}$ is a point for $-r_0 \le r \le \tilde{r}(D)$ and is a disk for $\tilde{r}(D) < r \le r_0$ with a generic Hopf bifurcation occuring at $\tilde{r} = \tilde{r}(D)$. The same remark applies to other elementary bifurcations that occur in one parameter families.

It will be apparent below that the proof of Theorem 1.1 is easily adapted to the following situation. Let $A = A(x)$ be a positive definite, continuous $n \times n$ matrix function uniformly for $x \in \Omega$ and let u^T be the transpose of an N-dimensional column vector. Consider the equation

$$(1.10)\qquad \begin{aligned} u_t &= D[\operatorname{div} A\nabla u^T]^T + f(x,u) \quad \text{in } \Omega \\ [A\nabla u^T]^T n &= E(u) \quad \text{in } \partial\Omega \end{aligned}$$

where n is the outward unit normal vector to $\partial\Omega$, $f \in C^{1,1}(\Omega \times \mathbb{R}^N, \mathbb{R}^N)$ and

$$(1.11)\qquad \begin{aligned} E(u) &= \int_{\partial\Omega} e(x,y)u(y)dy \\ e(x,y) &= \operatorname{diag}(e_1(x,y),\ldots,e_N(x,y)) \\ D|\Omega|^{-1}e &\to \tilde{e}, \quad \int_{\partial\Omega}\int_{\partial\Omega} \tilde{e} = \zeta \end{aligned}$$

where $e, \tilde{e}$ are continuous on $\partial\Omega \times \partial\Omega$. Let

$$(1.12) \qquad F(u) = |\Omega|^{-1} \int_\Omega f(x,u)dx.$$

Then Theorem 1.1 is valid with (1.4) replaced by (1.11), (1.1), (1.2) replaced by (1.10) and (1.5) replaced by

$$(1.13) \qquad \dot{u} = \zeta u + F(u)$$

It will be clear also form the proofs given below that Theorem 1.1 remains valid even if the equation (1.1), (1.2) is a functional differential equation; that is, $f: C([-r,0],\mathbb{R}^N) \to \mathbb{R}^N$ where $r > 0$ is a given constant. Also, one can consider the equation (1.1), (1.2) coupled with an ordinary differential equation, and obtain the version of (1.5) coupled with the same ordinary differential equation. This is illustrated in Section 4 for a problem in genetics of Busenberg and Mahaffy, [1]. One could also have a functional differential equation in (1.10).

2. Proof of Theorem 1.1.

We will use the notation introduced in Section 1. For a fixed constant $b > 0$ and a given continuous function $a: \partial\Omega \to \mathbb{R}$, consider the eigenvalue problem

$$
(2.1) \qquad \begin{aligned} b\Delta\phi &= \lambda\phi \quad \text{in } \Omega \\ \partial\phi/\partial n &= -a(x)\phi \quad \text{on } \partial\Omega. \end{aligned}
$$

Suppose $a(x) = a(x,b)$ and

$$
(2.2) \qquad \begin{aligned} & b\, a(x,b) \to \beta_1(x) \quad \text{as } b \to \infty \\ & \beta_1(x) \text{ continuous } \quad |\Omega|^{-1}\int_{\partial\Omega} \beta_1 = \sigma. \end{aligned}
$$

The smallest eigenvalue $\lambda_1(b,a)$ of this problem is characterized by the variational principle (see Courant and Hilbert [2 ,p. 398])

$$
(2.3) \qquad -\lambda_1(b,a) = \min\{\int_\Omega b|\nabla\phi|^2 dx + b\int_{\partial\Omega} a\phi^2 dx: \int_\Omega \phi^2 dx = 1\}
$$

Also, if $\phi_1(b,a)$ minimizes this functional, then $\phi_1(b,a)$ is an eigenfunction corresponding to $\lambda_1(b,a)$.

Lemma 2.1. *If (2.3) is satisfied, and $\lambda_k(b)$, $k = 1,2,\ldots$ are the eigenvalues of (2.1), then there are constants $b_0 > 0$, $\mu > 0$ such that,*

$$\lim_{b\to\infty}\lambda_1(b) = -\sigma$$

$$\lambda_k(b) \le -\mu b, \quad k \ge 2, \quad \text{for} \quad b > b_0.$$

Also, there is a normalized eigenfunction $\phi_1(b)$ such that $\phi_1(b) \to |\Omega|^{-\frac{1}{2}}$ as $b \to \infty$.

Proof: For any $\varepsilon > 0$ there is a $b_0 > 0$ such that $b > b_0$ implies

$$\sup_x |ba(x) - \beta_1(x)| < \varepsilon$$

Taking $u(x) = |\Omega|^{-\frac{1}{2}}$, it follows from (2.2) that

$$-\lambda_1 \le |\Omega|^{-1}\int_{\partial\Omega} ba = |\Omega|^{-1}\int_{\partial\Omega}(\beta a-\beta_1) + \sigma < \sigma+\varepsilon K$$

where $K = |\Omega|^{-1}|\partial\Omega|$.

The trace theorem for $W^{1,2}(\Omega)$ implies there is a constant c_0 such that

$$\int_{\partial\Omega}\phi^2 \le c_0\left[\int_\Omega |\nabla\phi|^2 + \int_\Omega \phi^2\right].$$

If we let $\sum \doteq \sup_x|\beta_1(x)|$ and $\phi_1(b,x)$ be an eigenfunction for $\lambda_1(b)$, $\int_\Omega \phi_1^2(b,\cdot) = 1$, then

$$\sigma + \varepsilon K > b \int_\Omega |\nabla\phi_1|^2 + b\int_{\partial\Omega} a\phi_1^2$$

$$= b \int_\Omega |\nabla\phi_1|^2 + \int_{\partial\Omega} (ba - \beta_1)\phi_1^2 + \int_{\partial\Omega} \beta_1\phi_1^2$$

$$> b \int_\Omega |\nabla\phi_1|^2 - (\textstyle\sum + \varepsilon)\int_{\partial\Omega} \phi_1^2$$

$$> [b - c_0(\textstyle\sum + \varepsilon)]\int_\Omega |\nabla\phi_1|^2 - (\textstyle\sum + \varepsilon)\, c_0\int_\Omega \phi_1^2$$

$$= [b - c_0(\textstyle\sum + \varepsilon)]\int_\Omega |\nabla\phi_1|^2 - (\textstyle\sum + \varepsilon)\, c_0$$

Thus, for $b > c_0(\sum + \varepsilon)$, we have

$$\int_\Omega |\nabla\phi_1|^2 < \frac{\sigma+\varepsilon K + c_0(\sum + \varepsilon)}{b - c_0(\sum + \varepsilon)} \overset{\text{def}}{=} \frac{c_1}{b-c_2}$$

Thus, $\int_\Omega |\nabla\phi_1(b,\cdot)|^2 \to 0$ as $b \to \infty$. Since the eigenfunction $\phi_1(b,x)$ is a C^2-function of x (see, for example, [3 ,4]), it follows that $\phi_1(b,x) \to |\Omega|^{-1/2}$ as $b \to \infty$ uniformly in $x \in \Omega$. From this, we conclude that $\int_{\partial\Omega} ba\phi_1^2 \to \sigma$ as $b \to \infty$. Thus, $-\lambda_1 \to \sigma$ as $b \to \infty$. This proves the first part of the lemma.

The second eigenvalue $\lambda_2(b)$ is characterized by the minimization problem (2.2) with the additional restriction $\int_\Omega \phi\phi_1 = 0$. Let $\mu_2(b) = -\lambda_2(b)/b$. Then

$$\mu_2(b) = \min\left\{\int_\Omega |\nabla\phi|^2 + \int_{\partial\Omega} a\phi^2 : \int_\Omega \phi^2 = 1,\ \int_\Omega \phi\phi_1 = 0\right\}$$

Suppose now there is a sequence $b_j \to \infty$ as $j \to \infty$ such that $\mu_2(b_j) \to 0$ as $j \to \infty$. If $\phi_2(b_j,\cdot)$ is the corresponding eigenfunction, $\int_\Omega \phi_2^2 = 1$, then, as above, one concludes that $\int_\Omega |\nabla\phi_2|^2 \to 0$ and $|\Omega|^{-1}\int_\Omega \phi_2 \to 0$ as $b \to -\infty$. Thus, $\phi_2(b,\cdot) \to 0$ as $b \to \infty$ which contradicts the fact that $\int_\Omega \phi_2^2 = 1$. Thus, there is a $b_0 > 0$ and a $\mu > 0$ such that $\mu_2(b) \geq \mu$ for $b \geq b_0$. This implies that $-\lambda_2(b) \geq \mu b$ for $b \geq b_0$. This completes the proof of the lemma.

Now let us consider the parabolic PDE

$$(2.4)\qquad \begin{aligned} \partial u/\partial t &= b\Delta u && \text{in } \Omega \\ \partial u/\partial n &= -a(x,b)u && \text{in } \partial\Omega \end{aligned}$$

Let $Y = L^2(\Omega,\mathbb{R})$, $D(A) = \{\phi \in W^{2,2}(\Omega,\mathbb{R})\colon \partial\phi/\partial n = -a(x,b)\phi \text{ on } \partial\Omega\}$ and $A\phi = -b\Delta\phi$, $\phi \in D(A)$. Then

$$\int_\Omega (Au)(x)v(x)dx = b\int_\Omega \nabla u(x)\cdot\nabla v(x)dx + b\int_{\partial\Omega} a(x,b)u(x)v(x)dx$$

for $u \in D(A)$, $v \in W^{1,2}(\Omega,\mathbb{R})$ and A is formally self-adjoint. It has a self-adjoint extension to $W^{1,2}(\Omega,\mathbb{R})$. Furthermore, $\sigma(-A)$ consists of the eigenvalues of (2.1).

Let Y^α, $0 \leq \alpha < 1$, denote the Banach spaces associated with the fractional powers of A. Then (2.4) generates an analytic semigroup e^{-At} in Y^α. For $t > 0$,

$$e^{-At} = \frac{1}{2\pi i}\int_{\Omega} (\lambda+A)^{-1} e^{\lambda t}\, dt$$

where Γ is a contour in the resolvent set $\rho(-A)$ with $\arg\lambda \to \pm\theta$ as $|\lambda| \to \infty$ for some constant $\theta \in (\pi/2,\pi)$.

Let $\lambda_1(b)$ be the first eigenvalue of (2.1) and let $\phi_1(x) = \phi_1(b,x)$ be the corresponding normalized eigenfunction. Let $\langle\phi,\psi\rangle = \int_0^1 \phi(x)\psi(x)dx$ and let

$$Y^{\alpha} = \tilde{Y} \oplus \tilde{Y}^{\perp}_{\alpha}, \quad \tilde{Y} = sp[\phi_1].$$

If $u \in Y^{\alpha}$, let $u = v\phi_1 + w$, $v = \langle\phi_1,u\rangle$. If u is a solution of (2.4), then

$$dv/dt = \lambda_1(b)v$$

$$\partial w/\partial t = b\Delta w \quad \text{in} \quad \Omega$$

and w satisfies the boundary conditions

$$\text{(2.5)} \qquad \partial w/\partial t = -a(x,b)w \quad \text{on} \quad \partial\Omega$$

Let us define $\tilde{A} = b^{-1}A|\tilde{Y}^{\perp}_{\alpha}$ as $\tilde{A}w = \Delta w$ with the boundary conditions (2.5) for $w \in D(\tilde{A}) = D(A) \cap \tilde{Y}^{\perp}_{\alpha}$. Then $\tilde{A}$ is sectorial in $\tilde{Y}^{\perp}_{\alpha}$, and, by Lemma 2.1, $\sigma(\tilde{A}) > \mu$. Using [9 ,Theorem 1.5.4] we have for $w \in Y^{\perp}_{\alpha}$

$$|e^{-\tilde{A}t}w|_{Y^\alpha} \le k\ t^{-\alpha}e^{-\mu t}|w|_{L^2}, \quad t > 0$$

$$|e^{-\tilde{A}t}w|_{Y^\alpha} \le k\ e^{-\mu t}|w|_{Y^\alpha}, \quad t > 0$$

where k can be chosen to be independent of $b \ge b_0$. Then, making the transformation $t \to bt$, we obtain:

$$(2.6)\qquad \begin{aligned} |e^{-At}w|_{Y^\alpha} &\le k_1\ t^{-\alpha}\ e^{-\mu bt}|w|_{L^2}, \quad t > 0 \\ |e^{-At}w|_{Y^\alpha} &\le k_1\ e^{-\mu bt}|w|_{Y^\alpha}, \quad t > 0 \end{aligned}$$

with $k_1 > kb^{-\alpha}$, for $w \in \tilde{Y}_\alpha^\perp$ and $0 < \alpha < 1$, $b \ge b_0$.

Let us now return to the full equations (1.1), (1.2) and consider first the linear case $f = 0$. We are assuming that

$$|\Omega|^{-1}d_je_j(d_j,x) \to \tilde{e}_j(x), \quad \int_{\partial\Omega}\tilde{e}_j = \zeta_j$$

for $j = 1,2,\ldots,N$.

Let $\lambda_1(d_j)$ be the first eigenvalue of (2.1) with $(b,-a(b,\cdot)) = (d_j,e_j(d_j,\cdot)$ and $\tilde{\phi}_1(d_j,x)$ be a normalized eigenfunction and $\mu > 0$ such that the second eigenvalue $\lambda_2(d_j) \le -\mu d_j$ if $d_j \ge d_0$. If $d = \min(d_1,\ldots,d_N)$, then

$$\Lambda_D \to \zeta \quad \text{as} \quad d \to \infty$$

(2.7)
$$\Lambda_D = \mathrm{diag}(\lambda_1(d_1),\ldots,\lambda_N(d_N))$$

$$\zeta = \mathrm{diag}(\zeta_1,\ldots,\zeta_N)$$

Let

(2.8)
$$\Phi_D = \begin{bmatrix} \tilde{\phi}_1(d_1) & 0 & \cdots & 0 \\ 0 & \tilde{\phi}_1(d_2) & \cdots & 0 \\ \cdots & & & \\ 0 & 0 & \cdots & \tilde{\phi}_1(d_N) \end{bmatrix} \stackrel{\text{def}}{=} [\phi_1(d_1),\ldots,\phi_1(d_N)]$$

$$X^\alpha = (Y^\alpha)^N$$

and decompose X^α as

(2.9)
$$X^\alpha = U \oplus U_\alpha^\perp$$

$$U = \{\phi = \Phi_D v : v \in \mathbb{R}^N\}$$

$$U_\alpha^\perp = \{\psi \in X^\alpha : \langle\psi,\phi\rangle = 0 \quad \text{for all} \quad \phi \in U\}$$

where $\langle\phi,\psi\rangle = \int_\Omega \phi^T(x)\psi(x)dx.$

If $u(t,x)$ is a solution of (1.1), (1.2) written as (1.6), then v, w satisfy (1.7). The equation

$$\partial w/\partial t = D\Delta w$$

$$\partial w/\partial n = Ew \quad \text{on} \quad \partial\Omega$$

generates an analytic semigroup $T_D(t)$ on $U_\alpha^\perp$ which from (2.6) satisfies the estimates

$$|T_D(t)w|_{U_\alpha^\perp} \leq kt^{-\alpha} e^{-\mu dt}|w|_{U_0^\perp}, \quad t > 0,$$

$$|T_D(t)w|_{U_\alpha^\perp} \leq ke^{-\mu dt}|w|_{U_\alpha^\perp}, \quad t > 0.$$

Under the hypothesis of the theorem, the equation (1.5) has a compact attractor $A_{\zeta,f}$. As in [5], there is a Lipschitz continuous Liapunov function $V: \mathbb{R}^N \to \mathbb{R}$ such that, for any $v \in \mathbb{R}^N$ and $A_g = A_{\zeta,f}$,

(i) $V(v) = 0$ if $v \in A_g$

(ii) $a(d(v,A_g)) \leq V(v) \leq b(d(v,A_g))$ where $a(r)$ is continuous, nondecreasing, $a(r) > 0$ if $r > 0$ and $b(r)$ is continuous, $b(0) = 0$.

(iii) $\dot{V}_{(1.5)}(v) \leq -V(v)$ where

$$\dot{V}_{(1.5)}(v_0) = \overline{\lim}_{h\to 0^+} h^{-1}[V(v(h,v_0)) - V(v_0)]$$

with $v(t,v_0)$ being the solution (1.5) through v_0 at $t = 0$.

For any $c > 0$, let $V_c = \{v \in \mathbb{R}^N : V(v) < c\}$, $\overline{V}_c = C\ell\, V_c$. From (ii), $\overline{V}_c$ is compact for any $c > 0$. Assume now that $3/4 < \alpha < 1$ so that $L^\infty(\Omega,\mathbb{R}^N)$ is continuously embedded in X^α. As in Hale [5], we will show that, for any $c_1 < c$, there are δ, η, $\eta > \delta > 0$ and b_0 such that $v_0 \in V_{c_1}$, $|w_0|_{X^\alpha} < \delta$, $b \geq b_0$ imply that the solution $(v(t),w(t))$ of (1.7) through v_0, w_0 satisfies $u(t) = \phi_D v(t) + w(t) \in W_{c_1}$ for $t \geq 0$, where

$$W_{c_1} \overset{\text{def}}{=} \{u_0 = \phi_D v_0 + w_0,\ v_0 \in V_{c_1},\ |w_0|_{X^\alpha} < \eta\}.$$

Let $u(t,\cdot)$ be a solution of (1.1), (1.2) and let $u(t,\cdot) = \phi_D(\cdot)v(t) + w(t,\cdot)$, $v(t) \in \mathbb{R}^N$, $w(t,\cdot) \in U_\alpha^\perp$. Then:

$$dv/dt = P(v,w)$$

$$(2.10)\qquad \partial w/\partial t = D\Delta w + Q(v,w) \quad \text{in } \Omega$$

$$\partial w/\partial n = Ew \quad \text{on } \partial\Omega$$

where

$$P(v,w) = \Lambda_D v + \int_\Omega \phi_D(x) f(\phi_D(x)v + w(x))dx$$

$$Q(v,w)(x) = f(\phi_D(x)v + w(x)) - \phi_D(x)\int_\Omega \phi_D(y) f(\phi_D(y)v + w(y))dy.$$

Transforming $v \to |\Omega|^{\frac{1}{2}}v$, and using the variation of constants formula, we rewrite this as

$$\begin{aligned} &dv/dt = \zeta v + f(v) + [|\Omega|^{-\frac{1}{2}}P(|\Omega|^{\frac{1}{2}}v,w) - \zeta v - f(v)], \quad v(0) = v_0 \\ (2.11)\quad & \\ &w(t) = T_D(t)w_0 + \int_0^t T_D(t-s)Q(|\Omega|^{\frac{1}{2}}v,w)ds \end{aligned}$$

Since $\alpha > 3/4$, $\phi \in X^\alpha$ implies $\phi \in L^\infty(\Omega,\mathbb{R}^N)$ and there is a constant k such that $|\phi|_{L^\infty} \leq k|\phi|_{X^\alpha}$. Hence, there is an $\eta > 0$ such that $v_0 \in V_{c_1}$ and $|w_0|_{X^\alpha} < \eta$ imply $v_0 + w_0(x) \in \overline{V}_c$ for all $x \in \Omega$. Next, observe that

$$\begin{aligned} ||\Omega|^{-\frac{1}{2}}P(|\Omega|^{\frac{1}{2}}v,w) - \zeta v - f(v)| &= |(\Lambda_D - \zeta)v \\ &+ |\Omega|^{-\frac{1}{2}}\int_\Omega [\phi_D f(\phi_D|\Omega|^{\frac{1}{2}}v + w) - |\Omega|^{-\frac{1}{2}}f(v+w)] \\ &+ |\Omega|^{-1}\int_\Omega [f(v+w) - f(v)]| \leq \mu_1 + M_c|w|_{L^\infty} \\ &\leq M_c k|w|_{X^\alpha} + \mu_1. \end{aligned}$$

where $M_c = \sup\{|f'(v)|: v \in \overline{V}_c\}$ and $\mu_1 = \mu_1(d) \to 0$ as $d \to \infty$. In the same way, we obtain

$$\begin{aligned} |Q(|\Omega|^{\frac{1}{2}}v,w(x))| &\leq |f(\phi_D(x)|\Omega|^{\frac{1}{2}}v+w(x)) - f(v+w(x))| \\ &+ |f(v+w(x)) - f(v)| + |\phi_D(x)\int_\Omega \phi_D f(\phi_D v+w) - |\Omega|^{-1}\int_\Omega f(v+w)| \end{aligned}$$

$$+ |\Omega|^{-1}\int_\Omega |f(v+w) - f(v)| \le \mu_2|\Omega|^{-1/2} + 2M_c|w|_{L^\infty}$$

$$\le 2M_c k|w|_{X^\alpha} + \mu_2|\Omega|^{-1/2}$$

and

$$|Q(|\Omega|^{1/2}v,w)|_X \le 2M_c k|\Omega|^{1/2}|w|_{X^\alpha} + \mu_2$$

where $\mu_2 = \mu_2(d) \to 0$ as $d \to \infty$.

Then, for $v(t)$, $w(t)$ satisfying (2.10), if $v(s) \in V_{c_1}$, $|w(s)|_{X^\alpha} < \eta$ for $0 \le s \le t$, relations (2.11) imply that

$$\dot{V}(v(t)) \le -V(v(t)) + k_2||\Omega|^{-1/2}P(|\Omega|^{1/2}v,w) - \zeta v - f(v)|$$

$$\le -V(v(t)) + k_2 k M_c|w|_{X^\alpha} + k_2\mu_1$$

$$z(t) \le k_1 e^{-(\mu-\sigma)dt}z(0) + 2|\Omega|^{1/2}M_c k\ k_1\int_0^t (t-s)^{-\alpha}e^{-(\mu-\sigma)d(t-s)}z(s)ds$$

$$+ k_1\mu_2 e^{d\sigma t}\int_0^t (t-s)^{-\alpha}e^{-\mu d(t-s)}ds$$

$$\le k_1 e^{-(\mu-\sigma)dt}z(0) + 2|\Omega|^{1/2}k_1 k M_c L(\mu d)^{\alpha-1}y(t) + k_1\mu_2 L(\mu d)^{\alpha-1}d^{d\sigma t}$$

where k_2 is the Lipschitz constant for V on $\overline{V}_c$, $0 < \sigma < \mu$, $z(t) = |w(t)|_{X^\alpha}e^{\sigma dt}$, $y(t) = \sup\{z(s), 0 \le s \le t\}$ and $L = \int_0^\infty s^{-\alpha}e^{-(1-\sigma/\mu)s}ds$. Choosing $d \ge d_0$ such that $\theta = 1 - 2|\Omega|^{1/2}k_1 k\ M_c L(\mu d)^{\alpha-1} > 0$, we have

$$y(t) \le k_1\theta^{-1}[z(0) + \mu_2 e^{\sigma dt}]$$

where $\tilde{\mu}_2 = L(\mu d)^{\alpha-1}\mu_2$. This implies

$$\text{(2.12a)} \qquad |w(t)|_{X^\alpha} \leq k_1\theta^{-1}[e^{-\sigma dt}|w_0|_{X^\alpha} + \tilde{\mu}_2]$$

If $v(s) \in V_{c_1}$ and $|w(s)|_{X^\alpha} < \eta$ for $0 \leq s \leq t$, we also have:

$$\text{(2.12b)} \qquad \dot{V}(v(t)) \leq -V(v(t)) + k_2(kM_c\eta + \mu_1).$$

Let $V(v) \geq p > 0$ for $v \in \overline{V}_c \setminus V_{c_1}$, and choose $\eta > 0$ and d_0 so that:

$$P - k_2(k\, M_c\eta + \mu_2) > 0.$$

Then choosing δ and $d \geq d_0$ so that

$$k_1\theta^{-1}(\delta + \tilde{\mu}_2) < \eta,$$

relations (2.12) imply that, if $v_0 \in V_{c_1}$, $|w_0|_{X^\alpha} < \delta$, then $v(t) \in V_{c_1}$, $|w(t)|_{X^\alpha} < \eta$ for all $t \geq 0$. This finishes the proof of the claim.

Now let A denote the following subset of U:

$$A = \{\phi_D v : v \in A_{\zeta,f}\}.$$

Then $B \overset{\text{def}}{=} \{u_0 = \phi_D v_0 + w_0,\ v_0 \in V_{c_1},\ |w_0|_{X^\alpha} < \delta\}$ is a bounded neighborhood of A and the positive semiorbit $\gamma^+(B)$ is in W_{c_1}

and is precompact. Moreover, the estimate (2.12a) implies that, if d is sufficiently large, there exists a neighborhood $N(A)$ such that $B \subset N(A)$ and the ω-limit set $\omega(B)$ of B satisfies $\omega(B) \subset N(A)$, $\omega(B) = \bigcap_{t \geq 0} C\ell\, T_{D,E}(t)B$. Then, by the results in [7 , theorem 5.3], we obtain the existence of a compact attractor A_D in $N(A)$.

We want to prove that A_D is a manifold which is essentially the same as $A_{\zeta,f}$. To do this, we construct a local integral manifold $w = h(v,D)$, $v \in V_{c_1}$ of (1.7). If one extends $f|\overline{V}_c : \overline{V}_c \to \mathbb{R}^N$ to all $\mathbb{R}^N$ in such a way as to obtain a uniformly $C^{1,1}(\mathbb{R}^N, \mathbb{R}^N)$ function, the referred to integral manifold must satisfy the differential integral equation

$$\text{(2.13)} \qquad dv/dt = P(v,h(v,D)), \quad v(0) = v_0$$

$$\text{(2.14)} \qquad h(v_0,D) = \int_{-\infty}^{0} T_D(-s)Q(v(s),h(v(s),D))ds$$

where $v(s) = v(s,v_0,h)$ is the solution of (2.13) through v_0. In a more or less standard but technical way (see, for example, Henry [9] for PDE's and Hale [8] for ODE's), one uses the contraction mapping on an appropriate set of $C^{1,1}(\mathbb{R}^N, U_\alpha^\perp)$ functions $h(\cdot,D)$ to show that d_0 may be chosen large enough so that (2.13), (2.14) has a solution $h(v,D)$ for $d \geq d_0$. Restricting to $v \in V_{c_1}$, we obtain the positively invariant manifold

$$M_D = \{u = \phi_D v + h(v,D), \quad v \in V_{c_1}\}$$

Moreover, $h(v,D)$ and its derivative approach zero as $d \to \infty$, the manifold M_D is exponentially asymptotically stable and the flow on it is given by $(v(t),h(v(t),D))$ where $v(t)$, $v(0) = v_0 \in V_{c_1}$, is a solution of the ODE (1.9). Since $\Lambda_D \to \zeta$ and $\Phi_D \to |\Omega|^{-\frac{1}{2}}I$, it follows that the vector field in (1.9) appropriately rescaled $(v \to |\Omega|^{\frac{1}{2}}v)$ uniformly approaches $g(v,\zeta) = \zeta v + f(v)$ in (1.5). Thus, equation (1.9) has an attractor B_D in V_{c_1}. The attractor $A_{\zeta,f}$ of (1.5) is upper semicontinuous (see [7]) and so $\lim_{d\to\infty} B_D \subset A_{\zeta,f}$. The attractor A_D for (1.7) is given by

$$A_D = \{u:\ u = \Phi_D v + h(v,D),\quad v \in B_D\}$$

Since $h(v,D) \to 0$ as $d \to \infty$, this completes the proof of Theorem 1.1.

3. A scalar example in one dimension.

Consider the scalar equation

$$(3.1)\qquad \partial u/\partial t = du_{xx} + f(u), \quad 0 < x < 1,$$

with the boundary conditions

$$(3.2)\qquad \begin{aligned} u_x - \varepsilon_0 u &= 0 \quad \text{at} \quad x = 0 \\ u_x + \varepsilon_1 u &= 0 \quad \text{at} \quad x = 1 \end{aligned}$$

where $d > 0$ and $\varepsilon_j = \varepsilon_j(d)$ are constants such that

$$(3.3)\qquad d\,\varepsilon_j(d) \to \zeta_j, \quad j = 0,1, \quad \text{as} \quad d \to \infty.$$

The equation corresponding to (1.5) is

$$(3.4)\qquad dv/dt = -(\zeta_0 + \zeta_1)v + f(v)$$

Theorem 1.1 asserts that, if (3.4) has a compact attractor $A_{\zeta,f}$, then (3.1) has a compact attractor A_d if $d \geq d_0$, d_0 sufficiently large. Furthermore, if the flow for the scalar equation is structurally stable, then the flow on A_d is structurally stable and is equivalent to the one on $A_{\zeta,f}$. The attractors A_d and $A_{\zeta,f}$

are close after $A_{\zeta,f}$ is appropriately embedded inthe function space.

The purpose of this section is to indicate how the perturbed boundary conditions affect the flow on the attractor. To do this, let us impose some additional conditions on f which will ensure that (3.4) has an attractor for all ζ_0, ζ_1. More precisely, suppose that there is a $v_0 > 0$ such that

$$
\begin{aligned}
& vf(v) < 0 \quad \text{for} \quad |v| > v_0 \\
(3.5) \qquad & \\
& f(v)/v \to -\infty \quad \text{as} \quad |v| \to \infty
\end{aligned}
$$

For any ζ_0, ζ_1, Equation (3.4) has a compact attractor $A_{\zeta,f}$ which is an interval $I_{\zeta,f} = [\alpha,\beta]$ where α, β are the extreme zeros of $-(\zeta_0 + \zeta_1)v + f(v)$.

As a particular illustration suppose $f(v)$ has five simple zeros as shown in Figure 1.

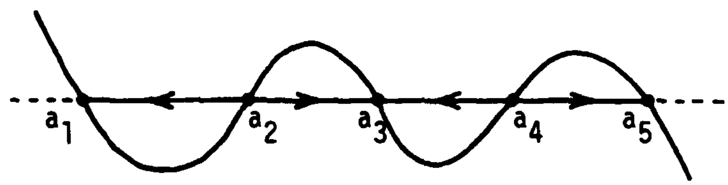

Figure 1

For Neumann boundary conditions and $d \geq d_0$, the attractor $A_{0,f}$ is the segment $[a_1,a_5]$ and the flow on the attractor is the one indicated in Figure 1. By varying ζ, it is clear that one can obtain each of the attractors shown in Figure 2. The perturbations in the boundary conditions induce large changes in the dynamical properties of the system.

Figure 2

The flow on the attractor in the function space for (3.1), (3.2) is the same as the ones indicated. However, the equilibrium points are not constant functions. The exact equilibrium points are not easy to compute since one must solve a nonlinear boundary value problem. Figure 3 in the (u,u_x)-plane indicates the approximate location of these equilibria for the case $\varepsilon_0 > 0$, $\varepsilon_1 > 0$. The line $L_0 = \{(u,u_x): u_x - \varepsilon_0 u = 0\}$ and the line $L_1 = \{(u,u_x): u_x + \varepsilon_1 u = 0\}$.

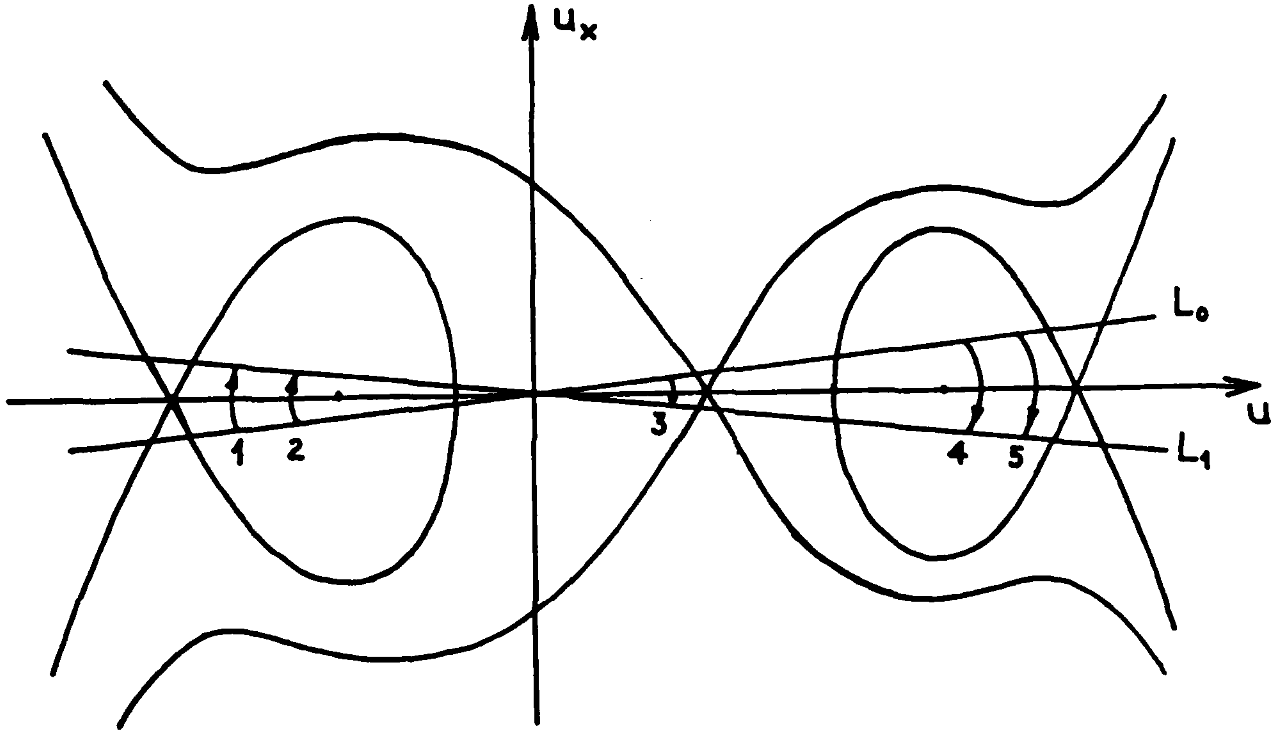

Figure 3

4. Two examples in genetic repression.

A simple model for genetic repression for control of biosynthetic pathways in cells is to consider two compartments within the cell wall separated by a permeable membrane (motivated by the work of Jacob and Monod [10]). The first compartment ω is regarded as a well mixed compartment (the nucleus) where mRNA is produced. The second compartment $\Omega \sim \omega$ consists of the cell in Ω minus the nucleus ω and represents the cytoplasm in which the ribosomes are randomly dispersed. It is in this region that

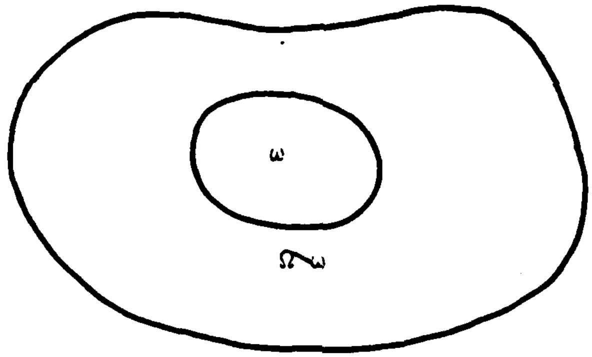

Figure 4

occurs the process of translation and consequent production of the repressor. The communication between the ribosome sites where translation occurs and the nucleus uses the process of diffusion in the cytoplasm

and transfer through the membrane bounding ω. This model was discussed in the one dimensional case by Mahaffy and Pao [11] and in the general case by Busenberg and Mahaffy [1].

Let u_i and v_i, $i = 1,2$ be respectively the concentrations of the mRNA and repressor protein in compartments ω and $\Omega \sim \omega$. The nucleus ω is considered as a well mixed compartment containing mRNA whose concentration u_1 is transcribed from the gene at a rate depending on the repressor protein v_1. The mRNA leaves ω and enters the cytoplasm $\Omega \sim \omega$ where it diffuses and interacts with the ribosomes. Through the delayed process of translation, a sequence of enzymes is produced which in turn produces a repressor v_2. This end product diffuses back to ω where it inhibits the production of u_1. The cell wall is a barrier through which neither biochemical substance can pass (see Figure 4).

Let $w_1 = \mathrm{col}(u_1,v_1)$, $w_2 = \mathrm{col}(u_2,v_2)$, $B = \mathrm{diag}\,(b_1,b_2)$, $A = \mathrm{diag}(a_1,a_2)$, $D = \mathrm{diag}(d_1,d_2)$, $C = (c_{ij})$, $c_{21} = c_0$, $c_{ij} = 0$ otherwise, $\beta = \mathrm{diag}(\beta_1,\beta_2)$, $F(w_1) = \mathrm{col}(f(v_1),0)$, where b_j, a_j, d_j, β_j, c_0 are positive constants and $f(v)$ is a decreasing function of v of the form $[1+v^\rho]^{-1}$ where $\rho > 2$ is a constant and $v \in \mathbb{R}$. Also, let $r_1 \geq 0$, $r_2 \geq 0$, be given constants. With this notation the two compartment model is

$$\frac{dw_1(t)}{dt} = F(w_1(t-r_1)) - Bw_1(t) + A\int_{\partial\omega}[w_2(t,y) - w_1(t)]dy$$

(4.1)

$$\frac{\partial w_2(t,x)}{\partial t} = D\Delta w_2(t,x) - Bw_2(t,x) + Cw_2(t-r_2,x), \quad x \in \Omega\sim$$

with the boundary conditions

$$(4.2) \qquad \frac{\partial w_2(t,x)}{\partial n} = -\beta[w_2(t,x) - w_1(t)] \quad \text{on} \quad \partial\omega$$

$$(4.3) \qquad \frac{\partial w_2(t,x)}{\partial n} = 0 \quad \text{on} \quad \partial\Omega.$$

where n denotes the outward normal to $\partial\Gamma$ with $\Gamma = \Omega\setminus\omega$.

The flow defined by these equations leaves the region $\mathbb{R}_+^4 = \{u_j > 0, v_j > 0,\ j = 1,2\}$ positively invariant (see Mahaffy and Pao [11]).

To apply the methods in the proof of Theorem 1.1, it is convenient to make a transformation of variables in (4.1), (4.2), (4.3):

$$w_1(t) \to W_1(t) \qquad w_2(t,x) \to W_2(t,x) + W_1(t).$$

The new equations are

$$(4.4) \qquad \frac{dW_1(t)}{dt} = F(W_1(t-r_1)) - BW_1(t) + A\int_{\partial\omega} W_2(t,y)dy$$

$$(4.5) \qquad \frac{\partial W_2(t,x)}{\partial t} = D\Delta W_2(t,x) - BW_2(t,x) - F(W_1(t-r_1))$$

$$+ CW_2(t-r_2,x) + CW_1(t-r_1,x) - A\int_{\partial\omega} W_2(t,y)dy$$

with the boundary conditions

$$\frac{\partial W_2(t,x)}{\partial n} = -\beta W_2(t,x) \qquad \text{on} \quad \partial\omega$$

(4.6)

$$\frac{\partial W_2(t,x)}{\partial n} = 0 \qquad \text{on} \quad \partial\Omega.$$

We also need the space in which we will consider (4.4), (4.5), (4.6). Let $X = L^2(\Omega \sim \omega, \mathbb{R}^2)$ and X^α, $0 \leq \alpha < 1$ be the usual fractional power space discussed before and associated with the Laplacian with boundary conditions $\partial u/\partial n = -\beta u$ on $\partial\omega$, $\partial u/\partial n = 0$ on $\partial\Omega$. Let X_+, X_+^α be the restrictions to the positive functions. Equations (4.4), (4.5), (4.6) then define a C^2-semigroup on $C([-r,0],\mathbb{R}_+^2) \times C([-r,0],X_+^\alpha)$.

As remarked earlier, the method of proof of Theorem 1.1 applies to this set of equations when $d = \min(d_1,d_2)$ is large and the β_j are functions of d_j, ζ_j so that

$$(4.7) \qquad |\Omega \sim \omega|^{-1}|\partial\omega| d_j \beta_j \to \zeta_j \qquad \text{as} \qquad d_j \to \infty$$

The resulting set of ordinary differential difference equations which are the analogue of equation (1.5) are

$$\frac{dW_1(t)}{dt} = F(W_1(t-r_1)) - BW_1(t) + A_1W_2(t)$$

(4.8)

$$\frac{dW_2(t)}{dt} = -\zeta W_2(t) - BW_2(t) + CW_2(t-r_2)$$

$$+ CW_1(t-r_2) - A_1W_2(t) - F(W_1(t-r_1)$$

where $\zeta = \mathrm{diag}(\zeta_1,\zeta_2)$, $A_1 = A$ [illegible].

Mahaffy and Pao [11] have shown that, for certain values of the parameters in (4.8), there is a globally attracting stable equilibrium point. Therefore, the attractor is a single point. They show also that a stable generic Hopf bifurcation occurs at this equilibrium point with the delays being used as the bifurcation parameter. Busenberg and Mahaffy [1] show that (4.4), (4.5), (4.6), for the diffusion coefficients large enough, must also have a generic Hopf bifurcation at approximately the same value of the delay parameters. This is proved by comparing the characteristic equations of the linear variational equations of (4.8) and (4.4), (4.5), (4.6) near their respective equilibria.

Let us now discuss the implications of our theory to this situation. Suppose ζ is fixed and that (4.8) has a compact attractor $\mathcal{A}_{\zeta,r_1,r_2}$ in $C([-r,0],\mathbb{R}_+^4)$. Under this assumption and, if (4.7) is satisfied, one can conclude that (4.4), (4.5), (4.6) has a compact attractor $\mathcal{A}_{D,\zeta,r_1,r_2}$ in $C([-r,0],X_+^\alpha)$ if $3/4 < \alpha < 1$ and $d \geq d_0$ where d_0 is sufficiently large. Furthermore, the flows on the two attractors are equivalent if the one on $\mathcal{A}_{\zeta,r_1,r_2}$ is structurally stable. Moreover, from the remarks made in the introduction, the Hopf bifurcation with respect to the delays referred to above occurs on $\mathcal{A}_{D,\zeta,r_1,r_2}$ if d is sufficiently large.

The following fact is also true even though it will neither be used here nor proved in detail. Since the only nonlinearity $F(v)$ in the equation is bounded together with its first and second derivatives, one can choose a global Liapunov function $V:C([-r,0],\mathbb{R}_+^4) \to \mathbb{R}$ for the

attractor $\mathcal{A}_{\zeta,r_1,r_2}$ as a quadratic form outside a large ball. This permits one to obtain a global attractor for (4.4), (4.5), (4.6).

The second example that we are going to consider is again a model in genetic repression with the same features as the one above, except that now the process of production of the repressor takes place in the membrane bounding the cell, looked upon as a third compartment $\tilde{\Omega}$. This model is also discussed in the one dimensional case by Busenberg and Mahaffy [1]. We need some new notation. Let u_i, v_i, $i = 1,2,3$ denote the concentrations of mRNA and repressor respectively in the compartments ω, $\Omega\sim\omega$ and the outside membrane $\tilde{\Omega}$. The compartments ω and $\tilde{\Omega}$ are considered well mixed. Let $w_i = \mathrm{col}(u_i, v_i)$, $i = 1,2,3$, and B, A, D, C, β, F be the same as above. Let also $\bar{A} = \mathrm{diag}(\bar{a}_1, \bar{a}_2)$, $\bar{\beta} = \mathrm{diag}(\bar{\beta}_1, \bar{\beta}_2)$ with $\bar{a}_j$, $\bar{\beta}_j$ positive constants. Then the three compartment model is

$$\frac{dw_1(t)}{dt} = F(w_1(t-r_1)) - Bw_1(t) + A\int_{\partial\omega}[w_2(t,x) - w_1(t)]dx$$

$$(4.9)\quad \frac{\partial w_2(t,x)}{\partial t} = D\Delta w_2(t,x) - B\, w_2(t,x), \qquad x \in \Omega\sim\omega$$

$$\frac{dw_3(t)}{dt} = -B\, w_3(t) + C\, w_3(t-r_2,x) + \bar{A}\int_{\partial\Omega}[w_2(t,x) - w_3(t)]dx$$

with the boundary conditions

$$\frac{\partial w_2(t,x)}{\partial n} = -\beta[w_2(t,x) - w_1(t)] \quad \text{on} \quad \partial\omega$$

$$(4.10)$$

$$\frac{\partial w_2(t,x)}{\partial n} = -\bar{\beta}[w_2(t,x) - w_3(t)] \quad \text{on} \quad \partial\Omega$$

The flow defined by these equations leaves the region $\mathbb{R}_+^6 = \{u_i > 0,\ v_i > 0,\ i = 1,2,3\}$ positively invariant. Again, it is convenient to make a transformation of variables in (4.9), (4.10) in order to obtain homogeneous boundary conditions. Let $\tilde{H} = \mathrm{col}(h_1,h_2,\bar{h}_1,\bar{h}_2)$ be the solution of the following boundary value problem with nonhomogeneous boundary conditions:

$$\Delta\tilde{H} = 0, \quad \text{in} \quad \Gamma = \Omega\sim\omega$$

$$\frac{\partial\tilde{H}}{\partial n} + \tilde{\beta}\tilde{H} = \tilde{\gamma}, \quad \text{on} \quad \partial\Gamma = \partial\Omega \cup \partial\omega$$

where $\tilde{\beta} = \mathrm{diag}(\beta_1,\beta_2,\beta_1,\beta_2)$, $\tilde{\gamma} = \mathrm{col}(\beta_1,\beta_2,0,0)$ on $\partial\omega$ and $\tilde{\beta} = \mathrm{diag}(\bar{\beta}_1,\bar{\beta}_2,\bar{\beta}_1,\bar{\beta}_2)$, $\tilde{\gamma} = \mathrm{col}(0,0,\bar{\beta}_1,\bar{\beta}_2)$ on $\partial\Omega$. Then, let $H = \mathrm{diag}(h_1,h_2)$, $\bar{H} = \mathrm{diag}(\bar{h}_1,\bar{h}_2)$ and introduce in (4.9), (4.10) the change of variables

$$w_1(t) \to W_1(t),\ w_2(t,x) \to W_2(t,x) + H(x)W_1(t) + \bar{H}(x)W_3(t),\ w_3(t) \to W_3(t)$$

If we let $G_\omega = \int_{\partial\omega} H$, $G_\Omega = \int_{\partial\Omega} H$, $\bar{G}_\omega = \int_{\partial\omega} \bar{H}$, $\bar{G}_\Omega = \int_{\partial\Omega} \bar{H}$, $A_1 = |\partial\omega|A$ and $\bar{A}_1 = |\partial\Omega|\bar{A}$, the new equations are

$$\frac{dW_1}{dt} = F(W_1(t-r_1)) - (\beta+A_1-AG_\omega)W_1(t) + A\int_{\partial\omega} W_2(t,y)dy + A\bar{G}_\omega W_3(t)$$

$$\frac{\partial W_2(t,x)}{\partial t} = D\Delta W_2(t,x) - B\, W_2(t,x)$$

(4.11)
$$- H(x)\{F(W_1(t-r_1)) - (A_1-AG_\omega)W_1(t) + A\int_{\partial\omega} W_2(t,y)dy + A\bar{G}_\omega W_3(t)\}$$

$$- \bar{H}(x)\{CW_3(t-r_2) - (\bar{A}_1-\bar{A}\bar{G}_\Omega)W_3(t) + \bar{A}\int_{\partial\Omega} W_2(t,y)dy + \bar{A}G_\Omega W_1(t)\}$$

$$\frac{dW_3(t)}{dt} = C\, W_3(t-r_2) - (B+\bar{A}_1-\bar{A}\bar{G}_\Omega)W_3(t) + \bar{A}\int_{\partial\Omega} W_2(t,y)dy + \bar{A}G_\Omega W_1(t)$$

with the boundary conditions

$$(4.12)\qquad \begin{aligned} \frac{\partial W_2(t,x)}{\partial n} &= -\beta\, W_2(t,x), \qquad \text{on } \partial\omega \\ \frac{\partial W_2(t,x)}{\partial n} &= -\bar{\beta}\, W_2(t,x), \qquad \text{on } \partial\Omega. \end{aligned}$$

These equations define a C^2 semigroup on $C([-r,0],\mathbb{R}^4_+) \times X^\alpha_+$ and we can apply again the method of proof of Theorem 1.1 when $d = \min(d_1,d_2)$ is large and $\beta_j,\bar{\beta}_j$ are functions of d_j,ζ_j so that

$$(4.13)\qquad |\Gamma|^{-1} d_j(|\partial\omega|\beta_j + |\partial\Omega|\bar{\beta}_j) \to \zeta_j \quad \text{as} \quad d \to \infty$$

If we denote by $\zeta = \operatorname{diag}(\zeta_1,\zeta_2)$, $G = |\Gamma|^{-1}\int_\Gamma H$ and $\bar{G} = |\Gamma|^{-1}\int_\Gamma \bar{H}$, the resulting set of ordinary differential difference equations are

$$\frac{dW_1(t)}{dt} = F(W_1(t-r_1)) - (B+A_1-AG_\omega)W_1(t) + A_1W_2(t) + A\bar{G}_\omega W_3(t)$$

$$\frac{dW_2(t)}{dt} = -(\zeta + B + GA_1 + \bar{G}\bar{A}_1)W_2(t)$$

$$(4.14)\qquad - GF(W_1(t-r_1)) + [GA_1 - GAG_\omega - \bar{G}\bar{A}G_\Omega]W_1(t)$$

$$- \bar{G}CW_3(t-r_2) + [\bar{G}\bar{A}_1 - \bar{G}\bar{A}\bar{G}_\Omega - GA\bar{G}_\omega]W_3(t)$$

$$\frac{dW_3(t)}{dt} = CW_3(t-r_2) - (B+\bar{A}_1-\bar{A}\bar{G}_\Omega)W_3(t) + \bar{A}W_2(t) + \bar{A}G_\Omega W_1(t)$$

This set of equations define a C^2-semigroup on $C([-r,0],\mathbb{R}_+^6)$ and it is this flow that should be compared to the one defined by the equations (4.9), (4.10).

As remarked earlier, Busenberg and Mahaffy [1] considered (4.9), (4.10) in one space variable and made a comparison to a set of equations which they claimed would correspond to a well mixed model. These equations were analogous to but not the same as (4.14).

For equations (4.9) and (4.10) to correspond to the physical problem, there must be some conservation laws and this imposes relationships between the constants A, $\bar{A}$, β, $\bar{\beta}$. Once these conditions are imposed, equations (4.14) in the one dimensional case take a simpler form. For special values of the parameters, one obtains the equations of Busenberg and Mahaffy [1]. The higher dimensional case always contains terms that depend on the shape of the region in a significant way. It is obvious that these equations need to be investigated in more detail.

References

[1] S. Busenberg and J. Mahaffy, "Interaction of Spatial Diffusion and Delays in Models," Preprint.

[2] R. Courant and D. Hilbert, "Methods of Mathematical Physics," Vol. I, Interscience, 1953.

[3] G. Folland, "Introduction to Partial Differential Equations," Mathematical Notes, Princeton Univ. Press, 1976.

[4] A. Friedman, Partial Differential Equations, Holt, Rinehart and Winston, 1969.

[5] J. K. Hale, "Large Diffusivity and Asymptotic Behavior in Parabolic Systems," LCDS Report #85-1, Brown University, January 1985.

[6] J. K. Hale, "Asymptotic Behavior and Dynamics in Infinite Dimensions," LCDS Report #84-28, Brown University, August 1984.

[7] J. K. Hale, L. Magalhães and W. Oliva, "An Introduction to Infinite Dimensional Dynamical Systems - Geometric Theory," Applied Math. Sciences, Vol. 47, Springer-Verlag, 1984.

[8] J. K. Hale, Ordinary Differential Equations, Wiley Interscience, New York (1969). Second Edition, Robert E. Krieger Publ. Co., 1978.

[9] D. Henry, "Geometric Theory of Semilinear Parabolic Equations." Lecture Notes in Math., Vol. 840, Springer-Verlag, 1981.

[10] F. Jacob and J. Monod, "On the Regulation of Gene Activity," Cold Spring Harbor Symp. Quant. Biol. 26 (1961), 193-211, 389-401.

[11] J. M. Mahaffy and C. V. Pao, "Models of Genetic Control by Repression with Time Delays and Spatial Effects," to appear in J. Math. Biol.